

76. (New) The purified antibody of claim 74, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.
77. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a polyclonal antibody.
78. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a monoclonal antibody.

RESPONSE

Pending claims

Claims 4-6, 29, 33 and 37-60 are pending. Claims 45-60 are withdrawn from consideration. Upon entry of this Amendment and Response, claims 4-6, 29, 33, 37-39, 41 and 61-78 are presented for consideration. A clean copy of claims 4-6, 29, 33, 37-39, 41 and 61-78 is provided for the Examiner's convenience.

Claims are canceled herein solely to expedite prosecution of the instant application and without prejudice to pursuing these claims in continuing and other related applications. No new matter is added by this amendment. Support for amended claims 4, 39 and 41 and newly added claims 61-78 are found throughout the specification, in the claims as originally presented and in the Figures. In particular, attention is directed to the present application at page 38, page 41, lines 3-8, page 40, line 25 through page 41, line 1, and page 57, lines 5-7. Support for antibodies which do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates may be found at least at page 38, lines 9-12. Support for antibodies that are generated against a polypeptide of at least about 5 amino acids of the amino acid sequence of SEQ ID NO. 4 may be found at page 44, lines 6-9, for example.

It is submitted that the amendments and newly added claims may be properly entered at this time, i.e., after final rejection, pursuant to 37 CFR §1.116, because the amendments do not raise any new issues or require a new search, and they reduce issues for appeal. Additionally, a number of claims have been cancelled.

Applicants thank the Examiner for his helpful comments during the telephonic interview of October 24, 2002. The amendments and newly added claims provided with this response are made to address the issues raised by the Examiner during the interview. It is believed that the amendments and newly added claims place the application in condition for allowance. Accordingly, entry of the amendments and newly added claims is earnestly solicited at this time.

Objection to the Specification

The Examiner has objected to the Specification and states that "Schematic A" provided on page 37 should be removed and provided in the form of a Figure.

Applicants provided with their previous Amendment and Response to Final Rejection new Figures 17 and 18, to provide formal drawings corresponding to Schematic A and B respectively and have amended the Brief Description of the Drawings and the specification, as appropriate, to reflect this change.

Applicants thank the Examiner for approving the drawings submitted with Applicants' previous Response filed October 8, 2002, as indicated by the Advisory Action mailed October 28, 2002. Applicants respectfully request entry of the amendments to the Specification to describe the newly added Figures.

Rejection of Claims 4, 6, 29 and 37 Under 35 U.S.C. § 102(b) (Buday)

Claims 4, 6, 29 and 37 are rejected under 35 U.S.C. § 102(b) as being anticipated by Buday, et al., *The Journal of Biological Chemistry* 269: 9019-9023, 1994 ("Buday").

The Examiner asserts that Buday teaches an antibody specific for phosphotyrosine which is a portion of SEQ ID NO. 4 and therefore that the antibody of Buday would bind to SEQ ID NO: 4.

Applicants respectfully traverse the rejection as it would be applied to the amended and newly added claims. As amended, claims 4-6, 29, 33, 37- 39, 41 and 61-66 recite antibodies that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4 and do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates. Claims 67-78 recite that the antibodies are generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

Unlike the antibodies of claims 4-6, 29, 33, 37- 39, 41 and 61-66, Buday's antibody *would* cross react with non-LAT ZAP 70 or non-LAT Syk substrates, since it would react non-specifically with *any* polypeptides comprising a phosphotyrosine group. Therefore Buday neither teaches nor suggests the antibodies of claims 4-6, 29, 33, 37- 39, 41 and 61-66.

With respect to claims 67-78, Buday's antibody is *not* generated against a portion of a LAT polypeptide comprising *at least about five amino acids of SEQ ID NO. 4*. This element of claims 67-78 must be given weight because the way in which the claimed antibodies are made *does* impact the structure and properties of the antibodies. The antigen-binding site of the claimed antibodies must recognize at least 5 amino acids of SEQ ID NO. 4 and must specifically

bind to a LAT polypeptide according to SEQ ID NO. 4 (i.e., the full length LAT polypeptide). There is no teaching or suggestion of antibodies with these properties anywhere in Buday. To the extent Buday's antibody might arguably recognize a phosphorylated tyrosine in a phosphorylated LAT polypeptide, it does not recognize a sequence of at least 5 amino acids of a LAT polypeptide according to SEQ ID NO: 4 and therefore does not have the same binding specificity required by claims 67-78.

Therefore, because Buday does not teach each element of the claims as required under 35 U.S.C. § 102, Buday does not anticipate the claims. See *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978) ("[r]jections under 35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the prior art.").

Applicants respectfully request that in view of the above arguments, the rejection should be reconsidered and withdrawn.

Rejection of Claims 4-5, 29 and 33 Under 35 U.S.C. § 102(e) (Hirth)

Claims 4-5, 29 and 33 stand rejected under 35 U.S.C. § 102(e) over Hirth, et al., U.S. Patent 5,058,959 ("Hirth"). The Examiner asserts that the antibody of Hirth is directed against a phosphotyrosine residue and as such, because the term "portion" reads on a single amino acid, Hirth allegedly anticipates the claims.

Applicants respectfully traverse the rejection as applied to the amended and newly added claims. As discussed above, as amended, claims 4-6, 29, 33, 37-39, 41 and 61-66 require that the antibodies recognize and *specifically* bind to a LAT polypeptide according to SEQ ID NO: 4 (i.e., a full length LAT polypeptide) and must *not cross react* with non-LAT ZAP 70 or non-LAT Syk substrates (i.e., non-LAT polypeptides which are phosphorylated by ZAP 70 and/or Syk).

Hirth's antibodies would non-specifically cross-react with any polypeptides comprising a phosphotyrosine, including non-LAT ZAP 70 or non-LAT Syk substrates. Additionally, Hirth neither teaches nor suggests antibodies which recognize and specifically bind to a full length LAT polypeptide according to SEQ ID NO: 4 and which are generated against a polypeptide which comprises at least about 5 amino acids of SEQ ID NO. 4 as claimed in claims 67-78. Hirth nowhere teaches or suggests antibodies with these properties.

Therefore, in view of the above arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claim 38 Under 35 U.S.C. § 112, First Paragraph

Claim 38 is rejected under 35 U.S.C. § 112, first paragraph. The Office Action expressly acknowledges that the specification is enabling for an antibody that binds a portion of SEQ ID NO:4. However, the position is taken that the specification does not reasonably enable an antibody that binds to "just any 20 amino acids" of SEQ ID NO:4 because antibodies generated against 20 amino acid fragments would not recognize the folded protein and as such would not be useful in detection. The Examiner concludes that it would require undue experimentation to use the claimed invention.

Applicants respectfully traverse the rejection. Antibodies are routinely generated against protein fragments and are routinely used in assays which do not rely on detecting tertiary conformations of proteins. For example, it was standard in the art at the time of filing (and still is) to perform Western blots of proteins electrophoresed on polyacrylamide gels comprising 10% SDS. In such gels, the proteins are denatured and do not retain the tertiary structure of the native protein. Yet Western blots have undeniable utility in assays which rely on the detection of specific proteins (e.g., such as in diagnostic assays). Additionally, antibodies generated against

LAT peptides are also able to recognize non-denatured proteins in Flow Cytometry Assays as well as in immunohistochemistry assays. Accordingly, Applicants respectfully submit that the rejection of claim 38 is improper and should be reconsidered and withdrawn.

Rejection of Claims 39-44 Under 35 U.S.C. § 112, First Paragraph

Claims 39-44 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner specifically objects to claims which recite "wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino-terminus, wherein said portion comprises at least 20 amino acids from" either the amino-terminus or carboxy-terminus. The Examiner asserts that "there is no support for antibodies that bind to at least 20 amino acids from the amino-terminal or carboxy-terminal."

Applicants respectfully submit that the rejection is moot in view of the deletion of the objected to language in the claims and traverse the rejection. Amended claim 39 recites that the polypeptide against which the antibodies are generated comprises the cytosolic tail of LAT. Support for this claim language may be found in the present application at page 40, line 25 through page 41, line 1. Amended claim 41 recites that the polypeptide against which the antibodies are generated comprises amino acids 31 to 233 of LAT. Support for the latter claim language may be found at least at page 57, lines 5-7. This sequence represents the sequence used as an immunogen to generate the antibodies disclosed in Applicants' Examples.

These amendments are made solely to expedite the prosecution of the instant application as Applicants respectfully submit that specification clearly states at page 40 that that the present invention is not limited to specific portions of LAT for the generation of antibodies. As such, claim 4 includes antibodies which recognize both N- and C-termini, as well as internal fragments of LAT and mutant forms of LAT.

In view of the above amendments and arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the claims are allowable and that the Application is now in condition for allowance. Applicants respectfully request early favorable action by the Examiner.

If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned agent of record.

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Marked-Up Version of Claims Showing Changes Being Made

4. A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.
39. (Amended) The purified antibody of any of Claims [Claim] 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises the cytosolic tail of LAT [wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino terminus, wherein said portion comprises at least 20 amino acids from the carboxy-terminus].
41. (Amended) The purified antibody of any of Claims [Claim 5] 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT [wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino-terminus, wherein said portion comprises at least 20 amino acids from the carboxy-terminus].

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PENDING CLAIMS UPON ENTRY OF AMENDMENT

4. (Amended) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.
5. A purified antibody of Claim 4, wherein said antibody is a polyclonal antibody.
6. The purified antibody of Claim 4, wherein said antibody is a monoclonal antibody.
29. The purified antibody of claim 4, wherein said antibody is directed against SEQ ID NO:4.
33. The purified antibody of claim 5, wherein the antibody is directed against SEQ ID NO: 4.
37. The purified antibody of Claim 6, wherein said antibody is directed against SEQ ID NO:4.
38. The purified antibody of Claim 4, wherein said portion comprises at least 20 amino acids of SEQ ID NO: 4.
39. (Amended) The purified antibody of any of Claims 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises the

cytostolic tail of LAT.

41. (Amended) The purified antibody of any of Claims 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.
61. (New) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4, wherein the at least a portion of the amino acid sequence comprises a phosphotyrosine residue and wherein the antibody specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.
62. (New) The purified antibody of Claim 61, wherein the at least a portion comprises at least about 5 amino acids of SEQ ID NO. 4.
63. (New) The purified antibody of Claim 61, wherein the at least a portion comprises at least about 20 amino acids of SEQ ID NO. 4.
64. (New) The purified antibody of Claim 61, wherein the at least a portion comprises of SEQ ID NO. 4.
65. (New) The purified antibody of any of Claims 61-64, wherein the antibody is a polyclonal antibody.
66. (New) The purified antibody of any of Claims 61-64, wherein the antibody is a monoclonal antibody.

67. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.
68. (New) The purified antibody of Claim 67, wherein the polypeptide comprising at least about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.
69. (New) The purified antibody of Claim 67, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.
70. (New) The purified antibody of Claim 68, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises the cytosolic tail of LAT.
71. (New) The purified antibody of Claims 70, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.
72. (New) The purified antibody of any of Claims 67-71, wherein the antibody is a polyclonal antibody.
73. (New) The purified antibody of any of Claims 67-71, wherein the antibody is a monoclonal antibody.
74. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4, wherein the at least about five amino acids comprises a phosphotyrosine residue and wherein the antibody

specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

75. (New) The purified antibody of claim 74, wherein the polypeptide comprising at least about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.
76. (New) The purified antibody of claim 74, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.
77. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a polyclonal antibody.
78. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a monoclonal antibody.